WHAT IS CLAIMED IS:

1. A method of representing biological pathways involved in the action of a drug in a cell type comprising:

(a) providing a drug response of said drug in said cell type, said drug response having been obtained by a method comprising measuring a plurality of cellular constituents in a cell of said cell type at a plurality of levels of exposure to said drug;

(b) representing a model drug response as a combination of one or more biological pathway responses in said cell type, wherein a biological pathway response in said cell type is the product of a method comprising measuring cellular constituents of said biological pathway in a cell of said cell type at a plurality of levels of a perturbation to said biological pathway, and wherein each of said one or more biological pathway responses in said combination are subject to an independent scaling transformation; and

(c) determining best scaling transformations of said one or more biological pathway responses which minimize the value of an objective function of the difference between said provided drug response and said model drug response,

whereby said combination of said one or more biological pathway responses subject to said best scaling transformations represents the biological pathways involved in the action of said drug in said cell type.

2. The method of claim 1 wherein said determining step (c) further comprises determining an actual minimized value of said objective function, said actual minimized value of said objective function being the minimized value of said objective function determined from said provided drug response and said model drug response, and wherein said method further comprises, after said determining step (c), steps of assessing the statistical significance of said best scaling transformations of said one or more biological pathways by a method comprising:

(d) obtaining an expected probability distribution of said minimized values of said objective function; and

(e) assessing the statistical significance of said actual minimized value of said objective function in view of said expected probability distribution of minimum values of said objective function.

3. The method of claim 2 wherein said step of obtaining said expected probability distribution of minimum values of said objective function comprises the steps of:

(i) randomizing said drug response with respect to said plurality of levels of drug exposure and randomizing said model drug response by randomizing said one or more biological pathway responses with respect to said plurality of levels of perturbation to said one or more biological pathways;

(ii) determining a theoretical minimum value of said objective function by finding best scaling transformations of said one or more randomized biological pathway responses which minimize said objective function of the difference between said randomized drug response and said randomized model drug response; and

(iii) repeating steps (i) and (ii) to determine a plurality of theoretical minimum values, said plurality of minimum values forming said expected probability distribution of minimized values.

4. The method of claim 1 further comprising, after said step of determining, a step of verifying that said one or more biological pathways are biological pathways actually involved in the action of said drug in said cell type by a method comprising:

(d) providing combined drug-perturbation responses in said cell type by a method comprising measuring a plurality of cellular constituents in a cell of said cell type exposed simultaneously to one or more levels of said exposure to said

drug and to one or more levels of perturbations in said one or more biological pathways; and

(e) selecting which of the following model responses behaves most similarly to said combined drug-perturbation responses:

(i) a first model response comprising said combination of said one or more biological pathway responses subject to said best scaling transformations evaluated at one or more first sums, each said first sum being the sum of one of said one or more levels of drug exposure subject to said scaling transformations and one of said one or more levels of perturbations to said biological pathways,

(ii) a second model response comprising said one or more second sums, each said second sum being the sum of said drug response evaluated at one of said one or more levels of drug exposure and said combination of said one or more biological pathway responses subject to said best scaling transformations evaluated at one of said one or more levels of perturbations to said biological pathways,

whereby said one or more biological pathways are verified as biological pathways actually involved in the action of said drug in said cell type if said first model response is selected.

5. The method of claim 1 further comprising, after said step of determining, a step of assigning a cellular constituent present in said drug response to the one of said one or more biological pathways in which said biological pathway response of said cellular constituent subject to its best scaling transformation has the greatest correlation with said drug response of said cellular constituent.

6. The method of claim 1 wherein said scaling transformations comprise transforming said levels of drug exposure to corresponding levels of said perturbations to said biological pathways.

7. The method of claim 6 wherein said transforming is by a linear mapping.

8. The method of claim 1 wherein scaling transformations are parameterized by sets of parameters.

9. The method of claim 8 wherein said objective function is minimized by selecting best sets of parameters for said scaling transformations.

10. The method of claim 1 wherein said objective function comprises a sum of the squares of differences of said drug response at said levels of exposure to said drug and said model drug response at said levels of exposure to said drug which are further subject to said scaling transformation.

11. The method of claim 1 wherein said objective function comprises the negative of the correlation of said drug response and said model drug response.

12. The method of claim 1 wherein said biological pathway responses are provided at levels of said perturbation to said biological pathways by a method comprising interpolating said measured values.

13. The method of claim 12 where said interpolating comprises approximation by a sum of spline functions.

14. The method of claim 12 where said interpolating comprises approximation by a Hill function.

15. The method of claim 1 wherein said one or more biological pathways in said cell type are chosen as being those biological pathways likely to be involved in the action of said drug in said cell type.

16. The method of claim 1 wherein said one or more biological pathways are chosen from a compendium of biological pathways present in said cell type.

17. The method of claim 1 wherein said cell type is substantially isogeneic to *Saccharomyces cerevisiae*.

18. The method of claim 1 wherein said cellular constituents comprise abundances of a plurality of RNA species present in said cell type.

19. The method of claim 18 wherein the abundances of said plurality of RNA species are measured by a method comprising contacting a gene transcript array with RNA from a cell of said cell type, or with cDNA derived therefrom, wherein a gene transcript array comprises a surface with attached nucleic acids or nucleic acid mimics, said nucleic acids or nucleic acid mimics capable of hybridizing with said plurality of RNA species, or with cDNA derived therefrom.

20. The method of claim 19 wherein said measuring cellular constituents in step (a) is performed by a method comprising contacting one or more gene transcript arrays (i) with RNA, or with cDNA derived therefrom, from said cell of said cell type that is exposed to said drug, and (ii) with RNA, or with cDNA derived therefrom, from said cell of said cell type that is not exposed to said drug, and

wherein said measuring cellular constituents in step (b) is performed by a method comprising contacting one or more gene transcript arrays (i) with RNA, or with cDNA derived therefrom, from said cell of said cell type that is exposed to said perturbations to said one or more biological pathways, and (ii) with RNA, or with cDNA derived therefrom, from said cell of said cell type that is not exposed to said perturbations.

21. The method of claim 1 wherein said cellular constituents comprise abundances of a plurality of protein species present in said cell type.

22. The method of claim 21 wherein the abundances of said plurality of protein species are measured by a method comprising contacting an antibody array with proteins from a cell of said cell type, wherein said antibody array comprises a surface with attached antibodies, said antibodies capable of binding with said plurality of protein species.

23. The method of claim 21 wherein the abundances of said plurality of protein species are measured by a method comprising performing two-dimensional electrophoresis of proteins from a cell of said cell type.

24. The method of claim 1 wherein said cellular constituents comprise activities of a plurality of protein species present in said cell type.

25. The method of claim 1 wherein said one or more biological pathways in said cell type comprise biological pathways originating at one or more specific cellular constituents, and wherein said perturbations to said biological pathways are performed by a method comprising modifying said one or more specific cellular constituents.

26. The method of claim 25 wherein said one or more specific cellular constituents are modified by a method comprising causing expression of said one or more specific cellular constituents under the control of a controllable expression system.

27. The method of claim 25 wherein said one or more specific cellular constituent are modified by a method comprising controllable transfection of genes expressing said one or more specific cellular constituents.

28. The method of claim 25 wherein said one or more specific cellular constituents are modified by a method comprising controllably decreasing abundances of RNA species encoding said one or more specific cellular constituents in a cell of said cell type.

29. The method of claim 28 wherein said method of controllably decreasing said abundances of RNA species comprises exposing a cell of said cell type to ribozymes targeted to cleave said RNA species.

30. The method of claim 25 wherein said one or more specific cellular constituents are modified by a method comprising controllably decreasing the rate of translation of RNA species encoding said one or more specific cellular constituents in a cell of said cell type.

31. The method of claim 30 wherein said method of controllably decreasing the rate of translation of RNA species comprises exposing a cell of said cell type to antisense nucleic acids or antisense nucleic acid mimics that hybridize to said RNA species or to DNA encoding said RNA species.

32. The method of claim 25 wherein said one or more specific cellular constituents are abundances of protein species or activities of protein species, and wherein said one or more specific cellular constituents are modified by a method comprising controllably decreasing said abundances in a cell of said cell type.

33. The method of claim 32 wherein said method of controllably decreasing said abundances comprises causing expression in a cell of said cell type of said one or more protein species as fusion proteins comprising said protein species and a degron, wherein said degron is controllable to increase the rate of degradation of said protein species.

34. The method of claim 32 wherein said method of controllably decreasing said abundances comprises exposing a cell of said cell type to antibodies, wherein said antibodies bind said protein species.

35. The method of claim 25 wherein said one or more specific cellular constituents are activities of protein species, and wherein said one or more specific cellular constituents are modified by a method comprising controllably decreasing said activities in a cell of said cell type.

36. The method of claim 35 wherein said method of controllably decreasing said activities comprises exposing a cell of said cell type to drugs which directly and specifically inhibit said activities of said protein species.

37. The method of claim 35 wherein said method of controllably decreasing said activities comprises exposing a cell of said cell type to dominant negative mutant protein species, wherein said dominant negative mutant protein species are proteins inhibiting said activities.

38. A method of determining a more pathway-specific drug candidate from an initial drug candidate comprising:

(a) representing the biological pathways involved in the action of an initial drug candidate by the method of claim 1;

(b) modifying the structure of said initial drug candidate;

(c) representing the biological pathways involved in the action of said modified initial drug candidate by the method of claim 1; and

(d) determining that said modified initial drug candidate is a more pathway-specific drug candidate than said initial drug candidate if said modified initial drug candidate has fewer biological pathways involved in its action than said initial drug candidate.

39. A method of identifying one or more specific biological pathways that are involved in the action of a drug and that mediate side-effects of the drug, said method comprising:

(a) carrying out the method of claim 1 for a first drug;

(b) carrying out the method of claim 1 for a second drug, wherein the first and the second drug are different and exhibit therapeutic efficacy for the same disease or disorder; and

(c) identifying those specific biological pathways involved in the action of said first drug that are different from those biological pathways involved in the action of said second drug, thereby identifying one or more specific biological pathways that are involved in the action of said first drug and that mediate side-effects of said first drug.

40. A method of identifying one or more specific biological pathways that are involved in mediating therapeutic efficacy for a disease or disorder, said method comprising:

(a) carrying out the method of claim 1 for a first drug;

(b) carrying out the method of claim 1 for a second drug, wherein the first and the second drug are different and exhibit therapeutic efficacy for the same disease or disorder; and

(c) identifying those specific biological pathways involved in the action of both said first drug and said second drug, thereby identifying one or more specific biological pathways that are involved in the action of said first drug and that mediate therapeutic efficacy for said disease or disorder.

41. A computer system for representing biological pathways involved in the action of a drug in a cell type comprising a processor and a memory coupled to said processor, said memory encoding one or more programs, said one or more programs causing said processor to perform a method comprising the steps of:

(a) receiving a drug response of said drug in said cell type, said drug response comprising measurements of a plurality of cellular constituents in a cell of said cell type at a plurality of levels of drug exposure;

(b) receiving one or more biological pathway responses, each of said one or more biological pathway responses comprising measurements of cellular constituents of said biological pathway in a cell of said cell type at a plurality of levels of a perturbation to said biological pathway;

(c) forming a model drug response as a combination of said one or more biological pathway, wherein each of said one or more biological pathway responses in said combination is subject to an independent scaling transformation;

(d) determining the value of an objective function of the difference between said drug response and said model drug response; and

(e) minimizing said determined value of said objective function by varying the scaling transformations of said one or more biological pathway responses to obtain best scaling transformations that minimize said determined value of said objective function;

whereby said combination of said one or more biological pathways responses subject to said best scaling transformations represents the biological pathways involved in the action of said drug in said cell type.

42. The computer system of claim 41 where said steps of receiving comprise making said drug response measurements and said biological pathway response measurements available in said memory.

43. The computer system of claim 41 wherein said forming a model drug response comprises adding said one or more biological pathway responses.

44. The computer system of claim 41 wherein said objective function comprises a sum of squares of the differences of

said drug response and said model drug response at said levels of drug exposure, said model drug response being provided at said levels of drug exposure by transforming by said scaling transformations said levels of drug exposure to corresponding levels of perturbations to each of said biological pathways and by interpolating said biological pathway responses to said corresponding levels of perturbations.

45. The computer system of claim 41 wherein said minimizing comprises performing the Levenberg-Marquandt method.

46. A method of measuring the similarity of the effects of two drugs on a cell type comprising:

(a) providing a first drug response of a first drug in said cell type, said drug response having been obtained by a method comprising measuring a plurality of cellular constituents in a cell of said cell type at a plurality of levels of exposure to said first drug;

(b) providing a second drug response for a second drug of interest in a cell type, said second drug response having been obtained by a method comprising measuring a plurality of cellular constituents in a cell of said cell type at a plurality of levels of exposure to said second drug; and

(c) determining the best scaling transformation of said biological pathway response which minimizes the value of an objective function of the difference between said drug response and said model drug response,

whereby said minimized value of said objective function provides a measure of similarity of the effects of said first and second drugs in said cell type.

47. A method of representing biological pathways involved in the effect of an environmental change upon a cell type comprising:

(a) providing an environmental response to said environmental change upon said cell type, said environmental

response having been obtained by a method comprising measuring a plurality of cellular constituents in a cell of said cell type at a plurality of degrees of severity of said environmental change;

(b) representing a model environmental response as a combination of one or more biological pathway responses in said cell type, wherein a biological pathway response in said cell type is the product of a method comprising measuring cellular constituents of said biological pathway in a cell of said cell type at a plurality of levels of a perturbation to said biological pathway, and wherein each of said one or more biological pathway responses in said combination are subject to an independent scaling transformation; and

(c) determining best scaling transformations of said one or more biological pathway responses which minimize the value of an objective function of the difference between said environmental response and said model environmental response,

whereby said combination of said one or more biological pathway responses subject to said best scaling transformations represents the biological pathways involved in the effect of said environmental change upon said cell type.

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